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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,934	07/14/2003	Laurens Nicolaas Sierkstra	4322.230-US	6607

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NOVOZYMES NORTH AMERICA, INC.
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SUITE 1600
NEW YORK, NY 10110

EXAMINER

MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
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1656

MAIL DATE	DELIVERY MODE
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05/09/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/618,934

Applicant(s)

SIERKSTRA ET AL.

Examiner

William W. Moore

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 February 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 88-97 and 99-117 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 88-97 and 99-117 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection on 15 February 2007. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 18 December 2006 has been entered.

Response to Amendment

Applicant's amendments and claim cancellations, as well as the Statement of Sameness according to CFR 1.821(e), filed 18 December 2006, overcome the objections of record of claims 96, 19, 102, and 106 herein, and to the specification, where amendment of the text of the Drawing Description of Figure 1 of specification is APPROVED. Applicant's Terminal Disclaimer filed 18 December 2006 is APPROVED, removing the bases for the double-patenting rejections of record herein over the claims of U.S. Patents 5,837,517, US 6,190,900, and US 6,682,924. Other rejections of record, however, are maintained for the reasons set forth below. This communication is not made final because new grounds of rejection are stated herein.

Claim Objections

Claims 96, 102, and 106 are objected to because of the following informalities: Clauses (b) of claims 96 and 102, and the beginning of claim 106, were amended on 18 December 2006 to insert the phrase "a substitution at" to introduce a list of alternative substituents at the same position. The preposition "at" in these phrases is inappropriate because, while the position is the same, the variations are multiple. Appropriate correction is required, e.g., amending clauses (b) of claims 96 and 102 and the beginning of claim 106 to describe "a substitution selected from the group consisting of Y171A, Y171C, Y171G, Y171H, Y171I, Y171L, Y171M, Y171N, Y171P, Y171Q, Y171S, and Y171W."

Double Patenting: Non-Statutory

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Applicant's arguments in the Response of 18 December 2006 addressing obviousness-type double patenting rejections of record have been fully considered but they are not persuasive. Applicant argues at pages 9 and 10 of the Response that "the two-way analysis of obviousness is the proper test when a later filed improvement patent issues before an earlier filed basic patent", citing the two-way test for obviousness of claims set forth for a special circumstance by *In re Berg*.¹ Applicant points out that the earliest effective US filing date of the instant disclosure is 6 May 1996.² However, several US patents the claims of which are cited and applied in the remaining double-patenting rejections of record had issued on applications filed in the United States before 6 May 1996. Applicant's argument is not germane to these rejections of record and, where appropriate, their effective filing dates are indicated in the rejections below.

Without regard to the effective filing dates of US patents the claims of which are cited and applied in the double-patenting rejections of record, the primary consideration in making each nonstatutory double patenting rejection is a judicially created doctrine grounded in public policy to prevent both (i) unjustified or improper timewise extension of the "right to exclude" granted by a patent and (ii) possible harassment by multiple assignees. Expiry dates of current patents, and patents that may issue on copending applications, cited in the rejections of record are not relevant to the latter purpose of public policy where Applicant need not remain the sole assignee of the instant application, nor remain a sole assignee of the patents and co-pending applications cited in the rejection of record. Any overlapping of patent term requires that the rejections of record be maintained because the specific circumstances that invoke the "two-way test" defined by *In re Berg* are not presented in the prosecution of this application relative to prosecutions of the patents and co-pending applications cited in the rejections of record.

The court in *Berg* found that a "two-way test" is proper when (i) claims of an earlier-filed, "basic", application are rejected in view of the patented claims of a later-filed, "improvement" application and, (ii) where the administrative action of the USPTO dictates issue of the later-

¹ 46 USPQ2d 1226 (Fed. Cir. 1998). The two-way test requires that (1) claims of the pending application be obvious in view of the patented claims and, (2) the patented claims be obvious in view of the pending application claims. 46 USPQ2d at 1229. Unlike the circumstances of the prosecution of the instant application, the applications at issue in *Berg* were filed simultaneously, thus the appellate panel did not consider rejections made in an application that was a later-filed continuation of an earlier application.

² US application serial No. 08/642,987 was filed 6 May 1996, the identical disclosure of which is present in its continuation applications serial Nos. 09/120,577, filed 22 July 1998, 09/585,747, filed 6 June 2000, and the instant application 10/618,934, filed 14 July 2003.

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filed application as a patent before the earlier-filed application despite Applicant's diligence in prosecuting the earlier-filed application. Applicant points out no particular quality or quantity of "improvement" that distinguishes polypeptides described by the claims rejected herein from the polypeptides described by claims of patents, or described by claims of copending applications, cited in the rejections of record. The record does not show that Applicant was prevented from filing a continuation or divisional application presenting a claim rejected herein before (i) filing an application issuing as a patent the claims of which are cited and applied in a rejection of record maintained below or (ii) filing a pending, commonly-assigned application the claims of which are cited and applied a rejection of record maintained hereinbelow.

The applications that presented conflicting claims considered by the court in *Berg* were filed on the same date. Even if Applicant identifies and explains an "improvement" embodied by a polypeptide claimed in a later-filed patent, or in a copending, commonly-assigned, application, it is Applicant that decided when the instant application presenting the claims rejected below should be filed and Applicant could have decided to do so before Applicant filed the applications issuing as patents, as well as the copending, commonly-assigned, applications, the claims of which are now applied in the rejections of record. Applicant, not the administrative action of the USPTO, decided that later-filed applications should issue first as patents and that It is clear that the "one-way test" of obviousness type double-patenting, i.e., "whether the application claims are obvious over the patent claims", must be applied in the obviousness-type double patenting rejections herein. This is required by a public policy intended to prevent both (i) unjustified or improper timewise extension of the "right to exclude" granted by a patent and (ii) possible harassment by multiple assignees. 46 USPQ2d, at 1229. While the patented claims applied in rejections of record of claims pending herein were first presented in later-filed applications, one of ordinary skill in the art reading the patented claims would consider subtilase modifications of the patented claims to render obvious amino acid substitutions of the modified subtilases recited in the pending, rejected, claims.

1. Claims 88, 89, and 95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, and 4 of US Patent 5,631,217, which issued on an application first filed in the US on 20 December 1991. Although the conflicting claims are not identical, they are not patentably distinct from each other where modified subtilases and compositions of claims 88, 89 and 95 herein comprise a subtilase having a Y167W amino acid substitution of modified subtilases and compositions of the patented claims.

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2. Claims 88, 92, and 95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 34, 56, 90, 111, and 121-123 of US Patent 5,741,694, which issued on an application first filed in the US on 6 January 1989. Although the conflicting claims are not identical, they are not patentably distinct from each other where modified subtilases and compositions of claims 88, 92 and 95 herein comprise a subtilase having an amino acid substitution at position 194 of modified subtilases and compositions of the patented claims.

3. Claims 88-90 and 92-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 17-19, 23, 38-41, 45, 65-68 and 72 of US Patent 6,605,458. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-94 herein comprise amino acid substitutions at positions 167, 170 and 194 embraced by generic substitutions at subtilisin BPN'-correspondent position 167, 171, and 194 of modified subtilases and compositions of the patented claims that further comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 206, 218, 222, and 235.

4. Claims 88-90 and 92-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-12, 14, 20, 35-37, 39, 45, 60-62, 64, 70, 86-88, 90, 96, 111-113, 115, 121, 136-138, 140, 146, 161-163, 165, 171, 186-188, 190, 196, 211-213, 215, and 221 of US Patent 6,773,907. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise amino acid substitutions at positions 167, 170, and 194 embraced by generic substitutions at subtilisin BPN'-correspondent position 167, 171, and 194 of modified subtilases and compositions of the patented claims that further comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 194, 206, 218, 222, and 235.

5. Claims 88-90 and 93-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8, 9, and 22 of US Patent No. 6,777,218. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 93-95 herein comprise amino acid substitutions at positions 167 and 170 embraced by generic substitutions at subtilisin BPN'-correspondent positions 167 and 170 of modified subtilases and compositions of the patented claims that further comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 206, 218, 222, and 235.

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6. Claims 88-90 and 92-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-11, 13, 19, 33-35, 37, 43, 57-59, 61, 67, 81-83, 85, 91, 105-107, 109, 115, 129-131, 133, 139, 153-155, 157, 163, 177-179, 181, and 187 of US Patent 6,780,629. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise amino acid substitutions at positions 167, 170, and 194 embraced by generic substitutions at subtilisin BPN'-correspondent positions 167, 170, and 194 of modified subtilases and compositions of the patented claims that comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 194, 206, 218, 222, and 235.

7. Claims 88, 90, and 92-95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6 and 7 of US Patent 6,808,913, which issued on an application first filed in the US on 6 January 1989. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions comprising same of claims 88, 90, and 92-95 herein comprise amino acid substitutions at positions 170 and 194 embraced by generic substitutions at subtilisin BPN'-correspondent positions 170 and 194 of modified subtilases and compositions of the patented claims that comprise at least one ancillary modification or mutation at either of positions 222 or 235.

8. Claims 88-90 and 92-95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-22, 25, and 26 of US Patent 6,893,855. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise amino acid substitutions at positions 167, 170, and 194 embraced by generic substitutions at subtilisin BPN'-correspondent positions 167, 170, and 194 of modified subtilases and compositions of the patented claims that comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 194, 206, 218, 222, and 235.

9. Claims 88-90 and 92-95 remain rejected for reasons of record, under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 5, 8, 14, 18, 21, and 27 of US Patent 6,921,657. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise amino acid substitutions at positions 167, 170, and 194, embraced by generic substitutions at subtilisin BPN'-correspondent positions 167, 170, and

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194 of modified subtilases and compositions of the patented claims that comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 194, 206, 218, 222, and 235.

10. Claims 88-90 and 92-95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14 and 19 of US Patent 7,026,153. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise amino acid substitutions at positions 167, 170, and 194 embraced by the generic substitutions at subtilisin BPN'-correspondent positions 167, 170, and 194 of modified subtilases and compositions of the patented claims that comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 194, 206, 218, 222, and 235.

11. Claims 88-91 and 93-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4, 5, 7, 8, and 16 of US 7,098,017, which issued on an application first filed in the United States on 4 November 1997. This rejection was formerly a provisional double-patenting rejection based on claims of application serial No. 09/948,080, but the application claims are now patented claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because the recited substitutions at positions 167, 170 and 171 of modified subtilases and compositions of claims 88-91 and 93-95 herein are embraced by the particular substitutions at positions 167, 170, and 171 of modified subtilases and compositions of the patent claims that further comprise at least one ancillary substitution or deletion at one or more of positions 27, 36, 57, 76, 97, 101, 104, 120, 123, 206, 218, 222, 224, 235, and 274.

12. Claims 88-90 and 92-95 remain rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11 and 26 of US Patent 7,109,016. This rejection was formerly a provisional double-patenting rejection based on claims of application serial No. 09/931,701 but the application claims are now patented claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise substitutions at positions 167, 170, and 194 of modified subtilases and compositions of patent claims that further comprise at least one ancillary substitution or deletion at one or more of positions 36, 57, 76, 97, 104, 120, 206, 218, 222, and 235.

13. Claims 88-90 and 92-95 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25 and 27 of US Patent

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No. 7,192,757. This rejection was formerly a provisional double-patenting rejection based on claims of application serial No. 10/884,325 but the application claims are now patented claims. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88-90 and 92-95 herein comprise one or more of the generic substitutions at positions 167, 170, and 194 of modified subtilases and compositions of the patent claims that further comprise at least one ancillary substitution or deletion at one or more of positions 27, 36, 76, 97, 101, 104, 120, 123, 206, 218, 222, and 235.

The following rejections are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

14. Claims 88, 90, and 93-95 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16, 23, 26, 27, 41, 46, and 49-53 of copending application serial No. 10/699,394. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88, 90, and 93-95 herein comprise one or more of the generic substitutions at position 170 recited in the preamble of claim 16 of the copending application that further comprises at least one ancillary substitution or deletion at one or more of the positions 27, 57, 76, 120, 218, and 222 and detergent compositions comprising same.

15. Claims 88, 90, and 93-95 remain provisionally rejected for reasons of record under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 25, 28, 29, and 32-34 of copending application serial No. 10/896,177. Although the conflicting claims are not identical, they are not patentably distinct from each other because modified subtilases and compositions of claims 88, 90, and 93-95 herein are embraced by the generic substitutions at position 170 of modified subtilases and compositions of claims of the copending application that further comprise at least one ancillary substitution at one or more of positions 218 and 222 and detergent compositions comprising same.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

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Claims 88 and 89 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lilley et al., 1992, made of record herewith.

Lilley et al. anticipate the subject matter of claims 88 and 89 in disclosing the amino acid sequence of a subtilase of *Dichelobacter nodosus*, which is "a member of the subtilisin family of proteases" wherein a tryptophan is present at the position that corresponds to position 167 in the amino acid sequence of subtilisin BPN'. See the title and second paragraph of the abstract, and the tryptophan, "W", at position +216 in the amino acid sequence of Figure 3 that aligns with the tyrosine at position 167 in the subtilisin BPN' amino acid sequence in sequence search results generated with the region of the mature subtilisin BPN' between amino acid positions 150 and 210, inclusive, available in SCORE. Claims 88 and 89 do not require that a tryptophan be present at a particular position in the amino acid sequence of a particular subtilisin, only that tryptophan occur at a position identifiable by correspondence to a reference amino acid sequence in a molecule having a functional characteristic, serine protease activity, and having a structure identifiable by a skilled artisan as similar to a subtilase, a broad genus of secreted, monodomain, serine proteases. A new method of obtaining a known chemical compound having a required structural element would not render the compound patentable and the claims permit no distinction between the presence of tryptophan at the subtilisin BPN'-correspondent position 167 in the subtilase of Lilley et al. and its introduction by a person at this position where the result of its presence at the recited position is inherently that of its introduction therein.

Claims 88, 89, and 95 are rejected under 35 U.S.C. § 102(b) as being anticipated by Branner et al., US 5,631,217, of record.

Branner et al. anticipate the substitution of tryptophan, "W", for a tyrosine at the subtilisin BPN'-correspondent position 167, as well as detergent composition comprising the modified subtilase and a surfactant, meeting the limitations of claims 88, 89, and 95 herein. See the patent claims 1, 3, and 4.

Claims 96, 101, 102, and 105 are rejected under 35 U.S.C. § 102(e) as being anticipated by Rasmussen et al., US 6,110,884, of record.

Applicant's claim amendments in the Response filed 18 December add the substitutions Y171I and Y171L to those recited in clauses (b) of claims 96 and 102. This rejection addressing a substitution at the single subtilisin BPN'-correspondent position 171 is made under 35 U.S.C. § 102(e) because the preambles of claims 96 and 102 describe modified subtilases as having "one" or "both" of two substitutions. Rasmussen et al., cited and discussed at page 18 of the communication mailed 16 June 2006, disclose modification of the amino acid sequences of the *Bacillus lentus* subtilisins 309 and 147 with the amino acid substitutions Y171I, Y171L, Y171S, Y171Q, Y171N, and Y171H, where these substitutions of isoleucine, leucine, serine, glutamine,

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asparagine and histidine, are registered at the subtilisin BPN'-correspondent position 171, as well as detergent compositions comprising same, anticipating the subject matters of claims 96, 101, 102, and 105 herein. See, e.g., the patent claims 1-3 and 8.

Claims 96, 97, 101, 106, and 109 are rejected under 35 U.S.C. § 102(e) as being anticipated by Mulleners et al., US 6,287,841, made of record herewith.

This rejection addressing a substitution at the single subtilisin BPN'-correspondent position 136 is made under 35 U.S.C. § 102(e) because the preambles of claims 96 and 102 describe modified subtilases as having "one" or "both" of two substitutions. Mulleners et al., issuing on a US national stage filing of an International application filed 27 July 1993 and available as prior art to an invention claimed herein, disclose modification of the amino acid sequences of the *Bacillus lentus* subtilisins 309 and PB92 by multiple amino acid substitutions, including a substitution of cysteine for the glutamate at position 134 [E134C] in both subtilisins 309 and PB92, which corresponds to position 136 in the amino acid sequence of the mature subtilisin BPN', as well as detergent compositions comprising such modified *Bacillus lentus* subtilisins, meeting limitations of claims 96, 97, 101, 106, and 109 herein. See, e.g., col. 5, line 60, col. 8, lines 20-28, and claims 16, 17, and 22.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 96 and 99-117 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rasmussen et al. and Mulleners et al., cited above, in view of Branner et al., of record.

This rejection addresses combined modifications at the two positions in clauses (a) and (b) of claims 96 and 102 herein, extension of modifications at the subtilisin BPN'-correspondent position 171 to subtilisins of claims 106, 110 and 114 herein, as well as a further combinations of one or more amino acid substitutions of claims 99, 100, 103, 104, 107, 108, 111, 112, 115, and 116 herein, and detergent compositions comprising same of claims 101, 105, 109, 113, and 117 herein. The teachings of Rasmussen et al. and Mulleners et al., discussed above, are taken as before. Rasmussen et al. additionally teach modifying the amino acid sequences of the *Bacillus lentus* subtilisins 309 and PB92 with one or more of the amino acid substitutions S99G, V102A, V102N, V102Y, N212D, and M216S, that, when registered by correspondence

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with the amino acid sequence of subtilisin BPN', are the substitutions S101G, V104A, V104N, V104Y, and M222S, as well as detergent compositions comprising same. See, e.g., col. 5, line 33, through col. 6, line 6, and claims 3, 9-15, and 22. Branner et al. combining an amino acid substitution at the subtilisin BPN'-correspondent position 171 in generic subtilisin amino acid sequences with one or more further modifications, such as the amino acid insertion, *36D, and the amino acid substitutions K27R, H120D, and K235L where the subtilisin to be modified may be any of "subtilisin BPN' . . . subtilisin Carlsberg . . . subtilisin 309, subtilisin 147 . . . *Bacillus* PB92 protease" and several other subtilisins. See, e.g., claims 5 and 20 of the patent.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the amino acid sequence of any of the subtilisins 309, 147, BPN', Carlsberg, and PB92, e.g., according to claims 106, 110 and 114 herein, by introducing one of the amino acid substitutions Y171I, Y171L, Y171S, Y171Q, Y171N, and Y171H taught by Rasmussen et al. and to then prepare modified subtilisins of claims 99, 100, 103, 104, 107, 108, 111, 112, 115, and 116 herein by further introducing one or more of the S101G, V104A, V104N, V104Y, and M222S modifications of Rasmussen et al. of claims 106, and/or one or more of the K27R, H120D, and K235L substitutions and/or *36D insertion of Branner et al. according to claims and to prepare detergent compositions of claims 101, 105, 109, 113 and 117 herein comprising such multiply-modified subtilisins. This is because Branner et al. teach that amino acid substitutions at the subtilisin BPN'-correspondent position 171 may advantageously be combined with further amino acid modifications, including the K27R, H120D, and K235L substitutions and *36D insertion in a great variety of subtilisins and because Rasmussen et al. suggest that their amino acid substitutions are also advantageously combined. Such an artisan would have had a reasonable expectation of success in combining a Y171I, Y171L, Y171S, Y171Q, Y171N, and Y171H modification of Rasmussen et al. with one or more of the further amino acid sequence modifications made by both Rasmussen et al. and Branner et al. in any of the subtilisins BPN', Carlsberg, 309, 147, and PB92 because Branner et al. teach that many different subtilisin amino acid sequences are amenable to the introduction of multiple amino acid modifications, which be expected to confer their separate advantages on the modified subtilisin, and because such an artisan would have been motivated to do so in view of the increasingly crowded art of subtilisin modification at the time the invention was made.

It would also have been obvious to one of ordinary skill in the art at the time the invention was made to combine the E134C substitution of Mulleners et al. with any of the Y171I, Y171L, Y171S, Y171Q, Y171N, and Y171H substitutions taught by Rasmussen et al. in modifying any of the three *Bacillus lentus* subtilisins taught by either of Mulleners et al. or Rasmussen et al.

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according to claims 96 and 102 herein and to prepare a detergent composition comprising the resulting, modified subtilisin. This is because each of Mulleners et al. and Rasmussen et al. teach the advantages of the substitution modifications they made at the subtilisin BPN'-correspondent positions 134 and 171. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success in realizing the advantages of the substitutions taught by Mulleners et al. and Rasmussen et al. at each position in the resulting, modified, subtilisin, and such an artisan would have been motivated to do so in view of the increasingly crowded art of subtilisin modification at the time the invention was made.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.



William W. Moore

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